

### **REMARKS**

Applicant notes with appreciation the detail and thoroughness of the Office Action of 25 August 2006. This amendment is submitted to be fully responsive thereto. By way of this amendment, claims 1, 29, 36, and 41-42 have been amended to recite with greater clarity that the inventive method is directed to treating a subject having inflammation associated with neurotrauma or neuronal injury. Support for this amendment is found in the specification at page 12, lines 15 to 20, and at page 13, lines 11 to 18. As such, it is submitted that no new matter has been added by way of this amendment.

Claims 1, 4-7 and 29-42 are the claims pending and currently under examination in this case. Claims 2-3 and 8-28 have been canceled. Claims 1, 4-7 and 29-42 stand rejected under 35 U.S.C. §103(a) over various references cited by the Examiner.

#### **Remarks Directed to Rejection of Claims 1, 5-7, 29-30, 32-36 and 38-40 Under 35 U.S.C. §103(a) over Grilli et al. in view of Bakhshi et al. and Myseros et al.**

Applicant submits that the pending independent claims 1, 29, 36, and 41-42 and those that depend therefrom are now not obvious over Grilli et al. in view of Bakhshi et al. and further in view of Myseros et al on the basis that there is no reasonable expectation of success given the teachings of these prior art references and that, therefore, a *prima facie* case of obviousness has not been established.

Grilli et al teaches the use of selected non-steroidal anti-inflammatory (NSAID) compounds for the prevention and the treatment of neurodegenerative diseases. In particular, Grilli et al discloses and claims the application of the NSAID compounds only to a particular neuronal damage, glutamate receptor – mediated neuronal damage (page 1, lines 3-4). The glutamate receptor – mediated neurotoxicity is only one of the many types of neuronal damages that usually follow the mechanical deformation involved in an incidence of neurotrauma or

neuronal injury (C. H. Taylor, Injury Prevention, 2002 Dec;8 Suppl 4:IV33-6). As noted in Grilli et al, the NSAID compounds unexpectedly and independently of any anti-inflammatory properties show a protective activity against glutamate-induced neurotoxicity (page 5 lines 9-12, page 6 lines 24-27). (Emphasis Added) Therefore, Grilli et al does not teach, or on the alternative, specifically excludes, the teaching of utilizing properties of the NSAID compounds other than their anti-glutamate-induced-neurotoxicity property, such as their anti-inflammatory property, anti-apoptosis property, and or hemorrhage blockage property.

Applicant agrees with the Examiner that Bakhshi et al. “teaches the administration of CNS drugs via intrathecal catheter” (page 5). However, Bakhshi et al. discloses the application of the intrathecal catheter in the treatment of CNS tumors (Abstract) and “with special emphasis on brain tumors” (Introduction). Since a brain tumor is neither a sufficient nor a necessary component of neurotrauma or neuronal injury, the limitations of Grilli et al. are not bolstered by Bakhshi et al. with respect to treatment of neurotrauma as claimed.

The new citation of the Myseros et al. reference further emphasizes Applicant’s position that one of skill in the art would have no expectation of success given the combined teachings of the references.

As correctly pointed out by the Examiner, Myceros et al. is cited as teaching “that prevention and/or treatment of glutamate neurotoxicity (specifically by glutamate antagonists) results in improvement in both mortality and morbidity of patients.” (Emphasis Added) In addition, Myceros et al. teaches that N-methyl-D-aspartate (NMDA) antagonists are more effective in focal ischemic damage than global ischemic damage (page 263). Applicant submits that this reference again teaches that glutamate receptor – mediated neuronal damage is only one of the many types of neuronal

damages involved in neurotrauma or neuronal injury and that the effectiveness of NMDA antagonists is rather limited.

Applicant notes that the present claims describe treatment of “a subject having neurotrauma” or neuronal injury. Given the teachings of Grilli et al and Myseros et al. regarding the treatment of the glutamate-induced neurotoxicity but not the inflammation-induced neuronal damage, and the teaching of Bakhshi et al regarding the specifically limited application of intrathecal administration route to brain tumors, Applicant submits that one of skill in the art would not have a reasonable expectation of success intrathecally or intraventrically administering an NSAID in treating neurotrauma or neuronal injury so as to reduce the inflammation associated thereto. Thus, Applicant submits that no *prima facie* case of obviousness is established because, again, there is no expectation of success given the combined teachings of Grilli et al. and Myseros et al. Further, the Bakhshi et al. reference does not make up for the lack of such teachings since this reference is asserted only for the teaching of routes of administration to the CNS.

In view of the above remarks, reconsideration and the withdrawal of the rejection of claims 1, 5-7, 29-30, 32-36 and 38-40 under 35 U.S.C. §103(a) over Grilli et al. in view of Bakhshi et al. and further in view of Myseros et al. is solicited.

**Remarks Directed to Rejection of Claims 4, 31, 37  
and 41-42 Under 35 U.S.C. §103(a) Over Grilli et al. in View of  
Bakhshi et al. and Myseros et al. and Further in View of McGeer et al.**

Applicant hereby incorporates by reference the above with regard to the deficiencies of Bakhshi et al. and Myseros et al. McGeer et al. fails to bolster Bakhshi et al. and Myseros et al. with regard to the limitations detailed. Additionally, claims 4, 31 and 37 are submitted to be patentable as the result of dependency from an allowable base claim.

On the basis of the above remarks, reconsideration and withdrawal of the rejection as to claims 4, 31, 37 and 41-42 under 35 U.S.C. §103(a) over Grilli et al. in view of Bakhshi et al. and Myseros et al. and in further view of McGeer et al. is solicited.

Summary

Claims 1, 4-7 and 29-42 are the claims pending in this application. Each claim is believed to be in proper form and directed to allowable and patentable subject matter. Reconsideration and allowance of the claims is requested. Should the Examiner find to the contrary, he is respectfully requested to contact the undersigned attorney in charge of this application to resolve any remaining issues.

Respectfully submitted,

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